P960030

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

JAN 29 1998

Ms. Lydia Telep
Regulatory Submissions Specialist
Pacesetter, Incorporated
A St. Jude Medical Company
15900 Valley View Court
Sylmar, CA 91342

Re: P960030
Passive Plus® DX Endocardial, Steroid Eluting Pacing Leads
Models 1342T, 1343K, 1346T, and 1345K
Filed: September 9, 1996
Amended: February 10, March 17, June 3, and June 23, 1997, and January 6, 1998

Dear Ms. Telep:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the Passive Plus® DX Endocardial, Steroid Eluting, Passive-Fixation Pacing Leads, Models 1342T, 1343K, 1346T, and 1345K. This device is indicated for use in combination with a compatible pulse generator to provide permanent pacing and sensing in either the atrium (Models 1342T or 1343K) or ventricle (Models 1345K or 1346T). We are pleased to inform you that the PMA is approved subject to the conditions described below and in the "Conditions of Approval" (enclosed). You may begin commercial distribution of the device upon receipt of this letter.

The sale, distribution, and use of this device are restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (the act) under the authority of section 515(d)(1)(B)(ii) of the act. FDA has also determined that to ensure the safe and effective use of the device that the device is further restricted within the meaning of section 520(e) under the authority of section 515(d)(1)(B)(ii) insofar as the sale, distribution, and use must not violate sections 502(q) and (r) of the act.

In addition to the postapproval requirements in the enclosure, the postapproval reports must include the results of fatigue testing conducted out to 400 million cycles on the Passive Plus® DX leads within one month of test completion.

Expiration dating for this device has been established and approved at two (2) years.

CDRH will publish a notice of its decision to approve your PMA in the FEDERAL REGISTER. The notice will state that a summary of the safety and effectiveness data upon which the approval is based is available to the public upon request. Within 30 days of publication of the notice of approval in the FEDERAL REGISTER, any interested person may seek review of this decision by requesting an opportunity for administrative review, either through a hearing or review by an independent advisory committee, under section 515(g) of the act

Failure to comply with the conditions of approval invalidates this approval order. Commercial distribution of a device that is not in compliance with these conditions is a violation of the act.

You are reminded that, as soon as possible and before commercial distribution of your device, you must submit an amendment to this PMA submission with copies of all approved labeling in final printed form.

All required documents should be submitted in triplicate, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

PMA Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Boulevard
Rockville, Maryland 20850

In addition under section 522(a) of the act manufacturers of certain types of devices identified by the act or designated by FDA are required to conduct postmarket surveillance studies. FDA has identified under section 522(a)(1)(A) the above noted device as requiring postmarket surveillance.

Upon approval and within thirty (30) days of first introduction or delivery for introduction of this device into interstate commerce you will be required to submit to FDA certification of the date of introduction into interstate commerce, a detailed protocol which describes the postmarket surveillance study, and a detailed profile of the study's principal investigator that clearly establishes the qualifications and experience of the individual to conduct the proposed study. For your information, general guidance on preparing a protocol for a postmarket surveillance study is enclosed.

At that time you should submit five (5) copies to

Postmarket Studies Document Center
1350 Piccard Drive (HFZ-544)
Rockville, Maryland 20850

Within sixty (60) days of receipt of your protocol, FDA will either approve or disapprove it and notify you of the Agency's action in writing. Do not undertake a postmarket surveillance study without an FDA approved protocol.

Failure to certify accurately the date of initial introduction of your device into interstate commerce, to submit timely an acceptable protocol, or to undertake and complete an FDA approved postmarket surveillance study consistent with the protocol, will be considered violations of section 522.

In accordance with the Medical Device Amendments of 1992, failure of a manufacturer to meet its obligations under section 522 is a prohibited act under section 301(q)(1)(C) of the act (21 U.S.C. 331(q)(1)(C)). Further, under section 502(t)(3) of the act (21 U.S.C. 352(t)(3), a device is misbranded if there is a failure or refusal to comply with any requirement under section 522 of the act. Violations of sections 301 or 502 may lead to regulatory actions including seizure of your product, injunction, prosecution, or civil money penalties or other FDA enforcement actions including (but not limited to) withdrawal of your PMA

If you have any questions concerning postmarket surveillance study requirements, contact the Postmarket Surveillance Studies Branch, at (301) 594-0639

Under section 519(e) of the act (as amended by the Safe Medical Devices Act in 1990), manufacturers of certain devices must track their products to the final user or patient so that devices can be located quickly if serious problems are occurring with the products. The tracking requirements apply to (1) permanent implants the failure of which would be reasonably likely to have serious adverse health consequences; (2) life sustaining or life supporting devices that are used outside of device user facilities the failure of which would be reasonably likely to have serious adverse health consequences; and (3) other devices that FDA has designated as requiring tracking. Under section 519(e), FDA believes that your device is a device that is subject to tracking because it is a permanent implant whose failure would be reasonably likely to have serious adverse consequences for tracking.

FDA's tracking regulations, published in the FEDERAL REGISTER on August 16, 1993, appear at 21 CFR Part 821. These regulations set out what you must do to track a device. In addition, the regulations list example permanent implant and life sustaining or life supporting devices that FDA believes must be tracked at 21 CFR ' 821.20(b) and the devices that FDA has designated for tracking at 21 CFR ' 821.20(c). FDA's rationale for identifying these devices is set out in the FEDERAL REGISTER (57 FR 10705-10709 (March 27, 1991), 57 FR 22973-22975 (May 29, 1992), and 58 FR 43451-43455 (August 16, 1993))

If you have any questions concerning this approval order, please contact Lynette Gabriel at (301) 443-8243.

Sincerely yours,

Susan Alpert, Ph.D., M.D.
Director
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

P960030

Summary of Safety and Effectiveness

P960030

Pacesetter, Inc.
Passive Plus® DX Endocardial, Steroid Eluting,
Passive-Fixation Pacing Leads

Food and Drug Administration
Center for Devices and Radiological Health
Office of Device Evaluation
Division of Cardiovascular and Respiratory Devices

Passive Plus® DX Endocardial, Steroid Eluting, Passive-Fixation, Pacing Leads, Models 1342T, 1343K, 1346T and 1345K

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SUMMARY OF SAFETY AND EFFECTIVENESS

I. GENERAL INFORMATION

Device Generic Name:	Implantable, transvenous, endocardial, bipolar, steroid eluting, atrial and ventricular pacing leads.
Device Trade Name:	Passive Plus® DX Endocardial Steroid Eluting, Passive-Fixation Pacing Leads, Models 1342T, 1343K, 1346T and 1345K.
Applicant's Name and Address:	Pacesetter, Inc. A St. Jude Medical Company 15900 Valley View Court P.O. Box 9221 Sylmar, CA 91392-9221
Date(s) of Panel Recommendation:	None
PMA Number:	P960030
Date of Notice of Approval to Applicant:	January 29, 1998

II. INDICATIONS FOR USE

The Passive Plus® DX lead is designed for use in combination with a compatible pulse generator to provide permanent pacing and sensing in either the atrium (models 1342T and 1343K) or ventricle (models 1346T and 1345K).

III. DEVICE DESCRIPTION

The Passive Plus DX models 1342T, 1346T, 1343K and 1345K are transvenous, endocardial, steroid eluting, pacing leads with a microporous titanium nitride (TiN) coated electrode. The leads use tines at the distal tip as a passive fixation mechanism.

The distal electrode of these leads includes between 400 and 1,000 micrograms of dexamethasone sodium phosphate (a steroid) in a silicone rubber matrix. This combination of medical adhesive and steroid is referred to as a monolithic controlled release device (MCRD).

The models 1342T and 1346T leads are bipolar having two multifilar, MP35N conductor coils, one terminating at the tip and the other at the ring electrode. The ring electrode consists of platinum iridium (Pt-Ir) with a microporous TiN coating. The distal pacing electrode consists of a platinum-iridium (Pt/Ir) semi-sphere with a microporous TiN coating. Silicone rubber tubing is used to insulate both the inner and outer conductor coils. The outer insulation is coated with a thin layer of polyvinyl pyrolidone (PVP) to increase the lubricity of the lead during implant.

The models 1343K/1345K leads are unipolar versions of the model 1342T/1346T leads. Since the model 1343K/1345K are unipolar, they have only one conductor coil and do not include a proximal electrode.

The models 1342T and 1343K are atrial J-shaped leads, whereas models 1345K and 1346T are straight ventricular leads.

IV. CONTRAINDICATIONS

The use of the model 1342T, 1346T, 1343K or 1345K lead is contraindicated:

- in patients who are expected to be hypersensitive to a single dose of 1.0 milligram of dexamethasone sodium phosphate

The use of the model 1346T or 1345K lead is also contraindicated:

- in the presence of tricuspid atresia and in patients with mechanical tricuspid valves

V. WARNINGS

- Exercise extreme caution when testing leads.
- Use only battery-powered equipment during lead implantation and testing to protect against fibrillation which may be induced by alternating currents.
- Use only properly grounded line-powered equipment used in the vicinity of the patient during the implant procedure.
- Insulate lead connector pins from any leakage currents that may arise from line-powered equipment.

VI. PRECAUTIONS

- For single use only. Do not resterilize leads more than once.
- Do not sterilize the lead using an autoclave, gamma radiation, or ultrasonics.
- Before opening the lead package, confirm that it is compatible with the pulse generator to be implanted.

Storage and Handling

- The lead should be stored at temperatures between -5°C (23°F) and 55°C (131°F).
- The lead conductor and its insulating sheath may be damaged if subjected to extreme mechanical stress.
- Do not stretch, crush, kink or bend the lead as leads may be damaged by improper handling before and during implant or by excessive mechanical stress post-implantation.
- Do not bring the lead into contact with sharp objects which could puncture or otherwise compromise the insulation.
- Handle the lead only with powderless, sterile surgical gloves.

- Avoid handling the lead with any surgical tools such as hemostats, clamps or forceps.
- Leads have an electrostatic affinity for particulate matter; do not expose them to lint, dust or other such materials.
- Avoid touching or handling the lead tip electrode itself.
- Do not immerse the lead body in mineral oil, silicone oil or any liquid other than sterile saline or injectable fluid.
- Do not immerse the tip electrode in any fluid prior to implantation. Immersion of the electrode may cause a small amount of steroid to be prematurely eluted.

Implantation

- Lead implantation should be performed only when proper emergency facilities for cardioversion and/or defibrillation are available.
- If subclavian venipuncture is used for lead introduction, it is important to insert the lead as lateral as possible during entry of the lead into the vein.
- Perforation of the atrial or ventricular wall may cause phrenic nerve stimulation, diaphragmatic stimulation or in some instances, cardiac tamponade. Phrenic nerve or diaphragmatic stimulation may also be a result of lead position.
- Failure to use the anchoring sleeve may result in damage to the lead's insulation, conductor coil or both.
- The manipulation of any and all hardware while in the vascular system should be performed only under continuous fluoroscopic monitoring.

VII. ALTERNATIVE PRACTICES AND PROCEDURES

Other marketed implantable cardiac pacing leads with or without steroid may meet the needs of patients for whom the model 1342T, 1346T, 1343K and 1345K leads are intended.

VIII. MARKETING HISTORY

Approximately 580 model 1342T/1346T leads have been distributed in Western Europe through June 1997. The Passive Plus DX model 1342T, 1346T leads have not been withdrawn from marketing for any reason relating to the safety and effectiveness of the device. Commercial distribution of the model 1343K and 1345K leads has not yet been initiated.

IX. POTENTIAL ADVERSE EFFECTS OF THE DEVICES ON HEALTH

The Passive Plus DX clinical study involved 158 patients implanted with 161 model 1342T atrial leads and 215 patients implanted with 216 model 1346T ventricular leads. Cumulative implant duration for each lead model is as follows:

- 1342T: 17,988 days (mean implant duration 113.8 days, range 0 to 239 days).
- 1346T: 24,061 days (mean implant duration 111.9 days, range 1 to 239 days).

A total of 8 patient deaths were reported. None of these deaths were judged to be device or lead related.

Observed Adverse Events

Device related adverse event (AEs) observed during the clinical investigation are summarized in Tables 1 and 2.

TABLE 1: PASSIVE PLUS® DX MODEL 1342T, ATRIAL LEADS
(Cumulative Implant Duration = 590.93 Months)

DEVICE RELATED ADVERSE EVENTS[1]	NUMBER OF PATIENTS[2] (N=158)	PERCENTAGE OF PATIENTS (%)	NUMBER OF LEADS[2] (N=161)	ADVERSE EVENTS PER LEAD MONTH[3]
Difficulty with Lead Placement	1	0.6	1	0.00169
Lead Dislodgment	9	5.6	9	0.01523
Loss of Capture	1	0.6	1	0.00169
Loss of Sensing	2	1.3	2	0.00338
TOTAL ADVERSE EVENTS	**13**	**8.1**	**13**	**0.02200**

1. Device Related Adverse Events are defined as symptomatic or asymptomatic device related clinical events with potential adverse effects which require physician intervention.
2. The difference in the number of patients (N=158) and the number of leads included in adverse event calculations (N=161) is due the fact that one lead was replaced with another 1342T lead after the patient contaminated the sterile field, and two leads were replaced with active fixation leads, one due to repeated dislodgment and one due to difficulty with lead placement.
3. This rate is determined by dividing the number of adverse events by the cumulative implant duration (in months) for the given lead model.

TABLE 2: PASSIVE PLUS® DX MODEL 1346T VENTRICULAR LEADS
(Cumulative Implant Duration = 790.44 Months)

DEVICE RELATED ADVERSE EVENTS[1]	NUMBER OF PATIENTS[2] (N=215)	PERCENTAGE OF PATIENTS (%)	NUMBER OF LEADS[2] (N=216)	ADVERSE EVENTS PER LEAD MONTH[3]
Difficulty with Lead Placement	1	0.5	1	0.00127
Cardiac Perforation	1	0.5	1	0.00127
Lead Dislodgment	1	0.5	1	0.00127
Loss of Capture	1	0.5	1	0.00127
Increased Capture Thresholds	2	0.9	2	0.00253
Decreased Sensing Thresholds	2	0.9	2	0.00253
TOTAL ADVERSE EVENTS	**8**	**3.7**	**8**	**0.01012**

1. Device Related Adverse Events are defined as symptomatic or asymptomatic device related clinical events with potential adverse effects which require physician intervention.
2. The number of leads is one greater than the number of patients as a result of one patient receiving a second model 1346T lead after unsuccessful attempted implant of previous model 1346T lead.
3. This rate is determined by dividing the number of adverse events by the cumulative implant duration (in months) for the given lead model.

Potential Adverse Events

Adverse events which may occur with this type of device including those listed above, include:

- cardiac tamponade
- excessive bleeding
- phrenic nerve stimulation
- thrombosis
- diaphragmatic stimulation
- induced atrial or ventricular ectopy.
- loss of pacing and/or sensing due to dislodgment or mechanical malfunction of the pacing lead
- embolism
- infection

Acute complications reported with direct subclavian venipuncture include pneumothorax, hemothorax, laceration of the subclavian artery, arteriovenous fistula, neural damage, thoracic duct injury, cannulation of other vessels, massive hemorrhage and, rarely, death.

X. SUMMARY OF STUDIES

A. *Qualification of Assembled Leads*

A series of *in vitro* (laboratory) qualification tests were performed on Passive Plus DX leads. Passive Plus DX leads are identical to the commercially available Passive Plus TiN model 1242T/1246T non-steroid pacing leads (K951950) with three exceptions. The Passive Plus DX hollow pacing tip electrode contains the steroid, dexamethasone sodium phosphate, within the electrode and as a surface coating; the tip electrode is laser-welded instead of crimped; and the lead is post-cured at lower temperatures to avoid degradation of the steroid plug.

Because of the similarity between Passive Plus TiN leads and Passive Plus DX leads, the following tests were performed during qualification of the Passive Plus TiN leads and therefore were not repeated for the Passive Plus DX leads:

<u>Bipolar leads (models 1342T and 1346T)</u>

- Joint section
- Hypot
- Stylet Insertion
- Suture slide
- Stylet performance
- Temperature cycle
- Joint bond
- Durability
- Current Leak
- Crimps (distal)
- Connector insertion

<u>Unipolar leads (models 1343K and 1345K)</u>

- Air Leak
- Suture Sleeve Performance
- Current Leakage
- Deformation due to set screw
- Connector Evaluation(IS-1 fit)
- J Shape Stability
- Crimp Pull
- Crimp Joint Section
- IS-1 Offset (and soak)
- Winding Fatigue
- Winding
- Visual/Dimensional
- Stylet Performance
- Set screw Damage
- Temperature Cycling
- Joint Bond
- Durability
- IS-1 Dimensional

Qualification tests performed on the Passive Plus DX leads included:

1. Multiple Sterilization

Thirty packaged lead samples and electrode subassemblies were subjected to five complete sterilization cycles. The established acceptance criteria required were: packaging shall be free of any cracks, fogging and contamination; the sterile seal shall be intact and not exhibit any delamination; the lead and accessories shall be positioned within the tray per its applicable assembly drawings; the inspection will be documented on the respective build traveler; and, electrode assembly - the electrode tip and coated area shall not exhibit damage, peeling or discoloration. The packaging and leads successfully passed the inspection criteria. The electrode tip coating was intact and did not exhibit peeling or discoloration.

2. **UPS Shipping Test**
Five packaged leads were placed in a shipping container and subjected to the UPS shipping test NTSA project 1A. All leads met the established acceptance criteria which required: packaging shall be free of any cracks, fogging and contamination; the sterile seal was intact and did not exhibit any delamination; and project labeling was intact. The packaging successfully passed the test criteria and the sterile seal was not compromised. No damage occurred to the lead or electrode.

3. **Vibration**
Five leads were packaged and vibrated at frequencies between five and 500 Hz in each of three mutually perpendicular axes. All leads and packaging were visually inspected following the vibration testing and confirmed to be free of any damage such as breaks, tears, cracking or seal separation. The established acceptance criteria required were: the package shall not exhibit any abrasion, tearing, cracking, damage or compromise of the sterile seal; and leads and accessories shall be located within the package as shown in the respective top level drawing. Stylets and protector caps shall withdraw (or can be removed) easily from the lead. The leads successfully passed the inspection criteria.

4. **Visual Examination**
Thirty leads were visually examined using the unaided eye and at 7-30X magnification. All leads met the established acceptance criteria which requires an absence of any damage such as tears, cuts or fractures in the tubing; kinks, fractures, contamination, unevenness or separation of the conductor coil or any damage or contamination of the electrodes and connector; the electrodes shall exhibit surface conditions free of particulate or damage; and the steroid coating shall not appear damaged or discolored. The leads successfully passed the inspection criteria.

5. **Temperature Shock**
Ten leads were subjected to five continuous temperature shock cycles at temperatures of -55°C and +65°C with a maximum transition time of one minute between temperatures. Leads were visually inspected and underwent measurement of DC resistance and helix extension/retraction testing following the shock exposure. The established acceptance criteria required were: the lead shall not exhibit any cracking, bond separation, or discoloration; and, electrode assembly - the electrode tip and coated area shall not exhibit damage, peeling, or discoloration. The leads successfully passed the acceptance criteria.

6. **Temperature Storage**
Ten leads were placed in a controlled temperature chamber at 65^{0}C, +5/-0^{0}C for 96 hours, +4/-0 hours, and -25^{0}C, +0/-5^{0}C for 96 hours. Upon completion, the samples were cooled at room temperature for one hour, minimum, followed by a visual examination. The established acceptance criteria required were: the lead shall not exhibit any cracking, bond separation, or discoloration; and, electrode assembly - the electrode tip and coated area shall not exhibit damage, peeling or discoloration. The leads successfully passed the acceptance criteria.

7. **Lead Resistance**

Thirty lead conductors and electrodes were measured for lead resistance to verify that the leads met the DC resistance requirements of the engineering specification. The leads successfully passed.

8. **Tip Stiffness**

This test only applied to 1346T and 1345K leads. The testing measured the force exerted onto the ventricle by the lead tip. These measurements characterized the lead tip's stiffness. The established acceptance criteria required were: The maximum lead tip stiffness force shall not exceed 36 grams for bipolar leads and 24 grams for the unipolar lead. The five leads successfully passed the acceptance criteria.

9. **Lead Introducer**

Leads were subjected to two introducer tests, one method tested the lead passage through an introducer alone, another tested the guidewire passage through the introducer after the lead passed through the introducer. The established acceptance criteria required were: the maximum force required to pass a lead through its related introducer shall not exceed 180 grams (.4 lb); lead friction shall not cause the lead to bend and not pass through the introducer; the fins or tines of the electrode shall remain intact; and there shall be no damage to the lead or insulation after all insertion methods, and no flaking or peeling of material around the lead tip. The ten leads successfully passed the test criteria. The results were statistically evaluated and found marginal. The introducer force limits were evaluated and acceptance criteria was modified to 240 grams. The final limits provide a 95% probability that at least 99% of the leads meet the introducer requirements.

10. **"J" Shape Retention-37^{0}C.**

This testing only applied to "J" atrial leads to ensure that the lead retained proper shape and configuration after stylet insertion in body temperature. The established acceptance criteria required were: the dimensional measurement of the "J" shape shall fit within the minimum/ maximum ($20^0 \pm 10^0$) range of T2192 and T3367. The five leads successfully passed the acceptance criteria.

11. **Polarization Measurement**

The leads were tested to measure the polarization of fully assembled leads. The leads were carefully handled without contaminating or damaging the surface of the electrodes. The leads were tested per MI-107 in the appropriate mode for each model (bipolar/unipolar). The established acceptance criteria required were: bipolar leads - lead polarization shall be less than 0.25 volt; and unipolar leads - lead polarization shall be less than 0.15 volt. The ten leads successfully passed the acceptance criteria.

12. **Lead Pull**

The leads were examined with the unaided eye and from 7-30x as needed to verify that the lead is completely bonded and free of tears in the insulation or molded sections to determine the overall yield strength of the completed lead. The established acceptance criteria required were: no separation of bonds or tubing damage shall occur at a load of 2.0 lb. The five leads successfully passed the acceptance criteria. However, the statistical analysis of the pull test results did not provide the desired level of confidence (95%). The bonds were analyzed and it was found that the ring electrode did not have an adequate amount of primer to provide an optimum joint. The production operators were retrained to effectively apply primer to bond, as established in the current documentation. A second lot was assembled following the manufacturing instructions. All leads passed the minimum pull test requirement. The lot met the statistical requirements (95% probability that 99% of the product meets the minimum requirement).

13. Total Elution

The maximum content of drug elution from the lead electrode was verified. Dexamethasone sodium phosphate was extracted from the steroid plug per ES1423. The coated tip of the electrode was included in the extraction process. The total amount of the drug was then calculated per the Elution Study protocol. The established acceptance criteria required were: the amount of Dexamethasone sodium phosphate present shall not exceed 1mg. The 12 leads successfully passed the acceptance criteria.

14. Dimensional-Electrode

The leads were tested to ensure the dimensional characteristics of the electrodes met the requirements of their related drawing. The established acceptance criteria required were: all of the dimensional measurements shall comply with the related drawing; and a first article report shall be included. The 12 leads successfully passed the acceptance criteria. First article reports were filed.

15. Document Compliance

The Product Specification, Engineering Specification, Test Specification, User Manuals, Traveler, etc., were subjected to a direct comparison of product specifications, tolerances, etc. The established acceptance criteria required were: all Engineering Specifications, Product Specification, Test Specifications, and User Manuals/literature shall provide specifications and tolerances which are in agreement. All documentation as listed was reviewed and found to be in agreement.

All qualification tests for the Passive Plus DX leads were successfully completed with the following exceptions:

- Four of the five lead qualification samples were improperly exposed to a curing temperature of 115°C (maximum allowable: 70°C). As a preventive measure, Traveler and Manufacturing Instructions changes were made to prevent further occurrences. This departure from standard manufacturing procedures cannot bias the results in any manner. The only component that could possibly be adversely affected by the elevated temperature would be the steroid, which was not part of the qualification program. One additional manufacturing lot was processed at the correct temperature to provide additional assurance that the elevated temperature did not have any effect on the lead.

- The lead protector caps did not remain in their original position following sterilization and USP testing. A change to the placement of the cap was made and the leads were subjected to vibration testing and passed.

- As recorded in its respective traveler, the 1346T lead was made slightly shorter than the specified length. VA-807, Rev. A was changed to clarify the winding cut lengths.

B. *Bell Mouth Flex Test*

The intent of this study was to determine the mechanical integrity of Passive Plus DX leads 1342T, 1346T, 1343K and 1345K. Because of the similarity of the coil (material, wire size, pitch, filiarity, coil diameter) and tubing (material, durometer, and dimensions), between models 1343K and 1345K, only model 1343K was evaluated.

A total of 12 leads each of 1342T, 1346T and 1343K leads were subjected to "Bell Mouth" flex testing of both the lead body and the lead connector. This testing is based on the recommendation of the Lead Test Task Force of the CEN/CENELEC Joint Working Group on Active Implantable Medical Devices (prEN 45502-#). This testing is intended to simulate worst case in vivo loading conditions and to demonstrate that the lead will not be adversely affected by its intended long-term implant environment.

The lead body and lead connector portion were subjected to 47,000 and 82,000 flex cycles respectively. All samples were examined visually and tested electrically to confirm that no electrical or mechanical damage had occurred.

C. *Distal Tip Fatigue Test*

Distal tip fatigue testing was performed on the distal portion of 10 samples of each Passive Plus DX lead. Atrial (1342T and 1343K) and ventricular (1346T and 1345K) samples were subjected to flexing representative of that experienced by the distal portion of the lead during implantation. This testing is intended to evaluate the integrity and reliability of the transition areas between the distal tip electrode and the surrounding portions of the lead. Testing was designed to simulate the maximum stress the distal portion of the lead experiences during both atrial and ventricular implantation. To date, 40 lead samples (10 samples of each model 1342T, 1346T, 1343K and 1345K) have exceeded 220 million flex cycles with no electrical or mechanical failure. The distal tip flex testing will continue until the samples have reached 400 million cycles. A final report will be provided to FDA upon completion of this testing.

D. In vitro *Pacing Test for TiN Coated Electrodes*

The electrical, chemical and physical stability of the TiN coating after exposure to the electrical currents associated with cardiac pacing was evaluated by subjecting six Passive Plus TiN model 1242T pacing leads to an in vitro pacing test. The model 1242T is a bipolar endocardial pacing lead with TiN coated distal and proximal pacing electrodes. The TiN coating and electrode base material are the same as those used in the electrodes of Passive Plus DX leads. This testing is applicable to models 1342T, 1346T, 1343K and 1345K.

During the test, the six leads were immersed in body temperature (37°C) pseudo extracellular fluid (PECF) and paced at a high rate (110 pulses per minute) and high output (6 volts and 1.5 millisecond pulse width) for six months. At the conclusion of this test, the TiN coating was examined with scanning electron microscopy. No evidence of corrosion or structural changes was observed. Additionally, PECF was analyzed for corrosion products using inductively coupled plasma discharge, graphite furnace atomic absorption spectroscopy and cold vapor absorption spectroscopy. No metallic components were found, suggesting that no corrosion of any components occurred.

E. *Testing of the Monolithic Controlled Release Device (MCRD)*

1. Evaluation of Drug Elution Rate

The rate of elution of dexamethasone sodium phosphate from the MCRD used in Passive Plus DX leads was evaluated by placing multiple devices into water and determining the concentration of dexamethasone sodium phosphate in the solution at regular intervals using ultraviolet spectrophotometry. This evaluation indicates that in water, the steroid is eluted rapidly at first, with approximately 50% of the total amount released into the solution within two days. A representative elution profile for the testing performed in water is provided in Figure 1. The *in vivo* elution rate is expected to be slower due to more complex interactions with blood and tissue.

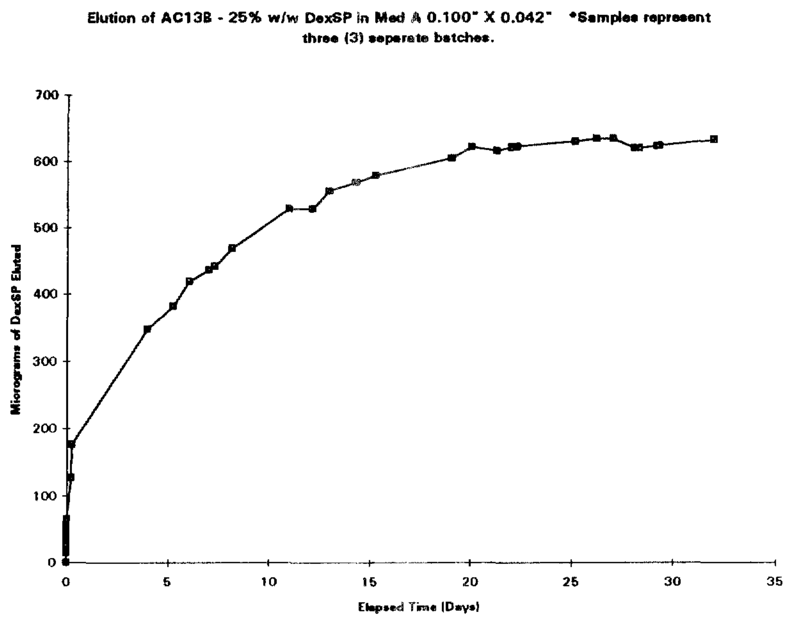

FIGURE 1: REPRESENTATIVE ELUTION PROFILE

2. Evaluation of Drug Stability/Shelf Life

The stability (over time) of the MCRD used in Passive Plus DX leads was evaluated by subjecting multiple samples to EtO sterilization and storing the samples at room temperature, 37°C and 50°C. Samples were evaluated at regular intervals by extraction into deionized water and analysis of the extraction solution using high pressure liquid chromatography (HPLC). A measurable conversion of the dexamethasone sodium phosphate to dexamethasone occurs at higher storage temperatures. Dexamethasone sodium phosphate does not convert to any species other than dexamethasone. At room temperature, it was estimated 13.1% of the dexamethasone sodium phosphate will be converted to dexamethasone after 14.5 months.

Since both dexamethasone sodium phosphate and dexamethasone are effective anti-inflammatory agents, the efficacy of the MCRD used in Passive Plus DX leads is not affected by long-term storage at elevated temperatures.

Labeling will state that the lead should be stored at temperatures between -5°C (23°F) and 55°C (131°F) and that expiration dating for the lead will be two years.

3. Evaluation of Multiple Sterilization on Drug Stability

Testing was performed to determine if multiple EtO sterilizations of the MCRD used in Passive Plus DX leads caused any undesirable chemical changes to the dexamethasone sodium phosphate. A total of 32 MCRD samples were subjected to five sequential sterilizations in EtO. An additional 32 samples were subjected to a single sterilization cycle as a control. Following sterilization, the samples were sectioned and placed in deionized water to extract any soluble contents of the MCRD. The extraction solution was analyzed using HPLC to identify the contents of the solution. The chromatographs for the samples subjected to the multiple sterilizations were compared to those of the control samples to allow identification of any changes due to exposure to multiple EtO sterilization cycles.

This evaluation revealed a small, but measurable increase in the conversion of dexamethasone sodium phosphate to dexamethasone in the samples subjected to five (rather than one) sterilization cycles. This increase was not significant. No evidence of any other species was detected in the extraction solution for either group.

Since both dexamethasone sodium phosphate and dexamethasone are effective anti-inflammatory agents, the results of this study indicate that the efficacy of the MCRD is not affected by multiple EtO sterilization cycles.

F. Evaluation Of Biocompatibility

The following materials used in Passive Plus DX leads come in contact with the patient's blood and/or tissue while the lead is implanted in the body:

- ETR silicone, 65 durometer (Q7-4765) and 80 durometer (Q7-4780)
- Pellethane 75D
- Pt-Ir
- TiN
- Dow Corning medical adhesive A
- Dexamethasone sodium phosphate
- MDX silicone (4516)
- Polyvinyl Pyrolidone

All blood/tissue contact materials used in Passive Plus DX leads (except for the silicone medical adhesive A used in the MCRD and dexamethasone sodium phosphate) have a long history of successful use in long-term implants and are identical to those materials used in Pacesetter Passive Plus TiN leads (K951950, K952206).

In addition to the extensive implant experience with these materials, standard biocompatibility testing (cytotoxicity, intracutaneous toxicity, acute systemic toxicity, intramuscular implants, hemolysis and USP pyrogen) have been performed according to guidelines contained in ISO-10933-1 for all blood/tissue contact materials, except for Pt-Ir. Biocompatibility testing for Pt-Ir was not deemed necessary due to its history of over 20 years of successful use as an electrode material for cardiac pacing leads.

In addition to standard biocompatiblity testing, more extensive testing, including chronic toxicity, guinea pig maximization (sensitization) and *Salmonella* reverse mutation assay (Ames) tests were performed for TiN. The dexamethasone sodium phosphate used in the MCRD is a marketed drug and therefore testing beyond that performed by the drug manufacturer and described in the approved NDA was not deemed necessary.

The results of biocompatibility testing performed for the blood/tissue contact materials of the Passive Plus DX leads, in addition to extensive clinical experience with these materials in long term cardiovascular implant applications, indicate that all materials used are biocompatible and therefore are safe for the intended application.

G. *Preclinical Animal Testing*

An animal evaluation of Passive Plus DX model 1342T atrial bipolar lead and 1346T ventricular bipolar lead was performed prior to the initiation of clinical investigations. This study involved 22 adult mongrel dogs, each implanted with one 1342T and one 1346T Passive Plus DX lead.

Each test subject had the electrode of one lead positioned at or near the apex of the right ventricle. The electrode of the second lead was positioned in or near the right atrial appendage. The connectors of both leads were inserted into a specially designed subcutaneous epoxy block to allow percutaneous measurement of lead electrical characteristics post implant.

Capture thresholds, intracardiac signal amplitude, and pacing impedance measurements were made using a Pacing System Analyzer (PSA) at implant and at 7(±1), 14(±2), 21(±2), 28(±2), 35(±2), 42(±2), 60(±5) days post implant, and monthly (±5 days) following the 60 day post implant measurements up to one year.

Atrial, bipolar mean capture threshold, recorded at a pulse width of 0.5 ms (milliseconds), did not exceed 0.6V throughout the one year implant for model 1342T. Ventricular, bipolar mean capture threshold, recorded at a pulse width of 0.5 ms, did not exceed 0.7V through the one year implant for model 1346T.

H. *Clinical Studies*

1. Introduction

A clinical investigation of Passive Plus DX model 1342T atrial bipolar lead and 1346T ventricular bipolar lead was conducted in the United States under approved IDE G950135. The investigation compared the Passive Plus DX steroid-eluting leads and the Passive Plus TiN non-steroid pacing leads models1242T/1246T (controls). A computer-generated 3:1 randomization scheme between Passive Plus DX leads and control leads was used to determine which lead(s) would be implanted into each patient.

The study enrolled patients of any age and either sex. Capture thresholds, sensing thresholds and impedances were measured in both the bipolar and unipolar configurations at implant, 14 days (±4 days), 30 days (±7 days), 90 days (± 14 days) and 180 days (±30 days) post implant. Data from 306 patients were analyzed. A total of 164 (54%) were males and 142 (46%) were females. The age of the patient population at the time of implant ranged from 20 to 92 years, with a mean of 74 ± 11 years.

The total number of investigational and control lead follow-ups included in the clinical data analysis is indicated in Table 3.

TABLE 3: IMPLANT AND FOLLOW-UP DATA RECEIVED

lead model	implant	2 weeks	1 month	3 months	6 months
1242T	42	35	33	23	4
1342T	156	139	132	80	11
1246T	80	72	75	48	6
1346T	215	192	177	106	19
total	**493**	**438**	**417**	**257**	**40**

2. Gender Bias Analysis

Overall, 46.0% of the patients included in the clinical investigation were female. This is comparable to the percentage of women in the general population who undergo pacemaker implantation (Sgarbossa et al, 1994; Shen et al, 1994; Tung et al, 1994), indicating that both sexes are appropriately represented in the study population.

3. Comparison of Investigational and Control Populations

The Fisher's Exact Test was applied to compare gender distribution for the control and investigational leads (for both the atrial and the ventricular leads). Primary Indications for Pacing were also examined for differences in distributions between the control and investigational groups. Similar tests were done for physiologic conditions affecting pacing thresholds and drugs affecting pacing thresholds, both at the time of implant. Student's t test was applied (two-tailed at the .05 significance level) to patient age at implant. The results are presented in Table 4. All p-values are larger than .05, indicating that statistically significant differences were not detected.

TABLE 4: COMPARISON OF PATIENTS WITH 1242T/1246T LEADS AND 1342T/1346T LEADS

VARIABLES	ATRIAL 1242T	ATRIAL 1342T	ATRIAL STATISTICS	VENTRICULAR 1246T	VENTRICULAR 1346T	VENTRICULAR STATISTICS
Gender: Male Female	21 (50%) 21 (50%)	88 (55.7%) 70 (44.9%)	Fisher's Exact Test p = 0.602	44 (55%) 36 (45%)	117 (54.4%) 98 (45.6%)	Fisher's Exact Test p = 1.000
Age (years): Range Mean Std Dev	38.2- 90.8 72.4 11.7	37.4 - 90.0 74.4 10.3	t = -1.0728 d.f. 198 p = 0.2847	20.8 - 92.3 74.1 13.4	33.5 - 92.0 74.3 9.8	t = -0.1105 d.f. 112.4 p = 0.9122
Primary Indication: Sick Sinus: Reported Normal[1]	13 (31.0%) 29 (69.1%)	48 (30.4%) 110 (69.6%)	Fisher's Exact Test p=1.000	27 (33.8%) 53 (66.3%)	62 (28.8%) 153 (71.2%)	Fisher's Exact Test p = 0.476
Sinus Brady: Reported Normal[1]	8 (19.1%) 34 (81.0%)	28 (17.7%) 130 (82.3%)	Fisher's Exact Test p = 0.824	10 (12.5%) 70 (87.5%)	35 (16.3%) 180 (83.7%)	Fisher's Exact Test p = 0.472
Heart Block: Reported Normal[1]	15 (35.7%) 27 (64.3%)	79 (50.0%) 79 (50.0%)	Fisher's Exact Test p = 0.118	30 (37.5%) 50 (62.5%)	93 (43.3%) 122 (56.7%)	Fisher's Exact Test p = 0.426
PCAPT: Condition(s) None Not Reported[2]	7 (16.7%) 35 (83.3%) 0	31 (19.8%) 126 (80.3%) 1	Fisher's Exact Test p = 0.826	17 (21.3%) 63 (78.8%) 0	43 (20.2%) 170 (79.8%) 2	Fisher's Exact Test p = 0.871
MAPT: Not reported at Implant Reported at Implant	34 (81.0%) 8 (19.1%)	125 (79.1%) 33 (20.9%)	Fisher's Exact Test p = 1.000	60 (75%) 20 (25%)	173 (80.5%) 42 (19.5%)	Fisher's Exact Test p = 0.336
TOTAL PATIENTS PER LEAD GROUP	**42**	**158**		**80**	**215**	

1. Normal Function, relative to the corresponding Primary Indication
2. Not included in statistical analysis

PCAPT = Physiological Conditions Affecting Pacing Thresholds
MAPT = Medications Affecting Pacing Thresholds

4. Effectiveness Data

Both unipolar and bipolar capture threshold data were analyzed separately for atrial and ventricular lead placement. A summary of this data is provided in Tables 5 and 6.

TABLE 5: ATRIAL CAPTURE THRESHOLDS (VOLTS) AT 0.4 MS PULSE WIDTH

Exam	unipolar: mean±SD (N)			bipolar: mean±SD (N)		
	1242T	1342T	P value†	1242T	1342T	P value†
implant	0.7±0.3 (39)	0.9±0.4 (141)	0.0672	0.8±0.3 (39)	0.8±0.4 (141)	0.6729
2 weeks	2.0±1.3 (32)	1.0±0.9 (129)	0.0001	2.0±1.3 (33)	1.0±1.0 (131)	0.0001
1 month	1.9±1.1 (28)	0.9±0.8 (120)	0.0001	2.0±1.3 (29)	1.0±0.7 (120)	0.0001
3 months	1.6±0.7 (20)	1.0±1.0 (71)	0.0001	1.4±0.7 (19)	1.0±0.9 (70)	0.0004

† Wilcoxon Rank Sum Test

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TABLE 6: VENTRICULAR CAPTURE THRESHOLDS (VOLTS) AT 0.4 MS PULSE WIDTH

Exam	unipolar: mean±SD (N)			bipolar: mean±SD (N)		
	1246T	1346T	P value†	1246T	1346T	P value†
implant	0.6±0.3 (78)	0.6±0.3 (208)	0.4055	0.7±0.4 (78)	0.7±0.3 (209)	0.7521
2 weeks	1.3±0.6 (68)	0.8±0.4 (189)	0.0001	1.6±0.8 (69)	0.9±0.5 (192)	0.0001
1 month	1.5±0.7 (75)	0.9±0.5 (174)	0.0001	1.7±0.7 (75)	1.0±0.5 (175)	0.0001
3 months	1.4±0.5 (48)	0.9±0.4 (105)	0.0001	1.6±0.6 (48)	1.0±0.4 (106)	0.0001

† Wilcoxon Rank Sum Test

At each follow-up visit, the mean capture thresholds for investigational Passive Plus DX models 1342T/1346T were lower than those of the control leads (Tables 5 and 6). In all cases, these differences were statistically significant with P values of 0.0004 or less.

5. Safety Data

A total of eight patients out of the population of 306 patients expired during the study. The deaths were unrelated to the implanted pacing leads.

One hundred and fifty-eight patients were implanted with an investigational atrial 1342T lead, and 215 patients were implanted with a investigational ventricular 1346T lead.

A total of 21 lead related adverse events were reported for the 377 model 1342T and 1346T leads implanted. Statistical analysis (Fisher's Exact Test, 2-Tailed) indicated no significant (p=0.154) difference in the adverse event rates for the investigational and control leads (see Table 7).

Of the 13 adverse events reported for model 1342T atrial lead, nine were lead dislodgements, two were related to loss of sensing, one was related to difficulty in placing the lead during implant, and one was related to loss of capture. Only one of the nine dislodged model 1342T leads was explanted.

Of the eight adverse events reported for model 1346T ventricular lead, one lead was cut during repositioning and was subsequently repaired, one was due to cardiac perforation, one was due to lead dislodgment, one was due to loss of capture, two were due to marked increase in capture thresholds, and two were due to marked decrease in sensing thresholds (see Table 8).

No unanticipated adverse effects were reported in association with either the model 1342T or 1346T lead.

TABLE 7: ATRIAL LEAD RELATED ADVERSE EVENTS

	MODEL 1242T (CUMULATIVE IMPLANT DURATION = 163.50 MONTHS)				MODEL 1342T[3] (CUMULATIVE IMPLANT DURATION = 590.93 MONTHS)			
DEVICE RELATED COMPLICATIONS[1]	NUMBER OF PATIENTS (N=42)	PERCENTAGE OF PATIENTS (%)	NUMBER OF LEADS (N=43)	ADVERSE EVENTS PER LEAD MONTH[4]	NUMBER OF PATIENTS[3] (N=158)	PERCENTAGE OF PATIENTS (%)	NUMBER OF LEADS[3] (N=161)	ADVERSE EVENTS PER LEAD MONTH[4]
Difficulty with Lead Placement	1	2.3	1	0.00612	1	0.6	1	0.00169
Lead Dislodgment	5	11.6	5	0.03058	9	5.6	9	0.01523
Loss of Capture	0	0	0	0.00000	1	0.6	1	0.00169
Loss of Sensing	1	2.3	1	0.00612	2	1.3	2	0.00338
DEVICE RELATED OBSERVATIONS[2]	NUMBER OF PATIENTS (N=43)	PERCENTAGE OF PATIENTS (%)	NUMBER OF LEADS (N=43)	ADVERSE EVENTS PER LEAD MONTH[4]	NUMBER OF PATIENTS[3] (N=158)	PERCENTAGE OF PATIENTS (%)	NUMBER OF LEADS[3] (N=161)	ADVERSE EVENTS PER LEAD MONTH[4]
Difficulty with Lead Placement	1	2.3	1	0.00612	0	0	0	0.00000
Loss of Capture	1	2.3	1	0.00612	0	0	0	0.00000
TOTAL ADVERSE EVENTS	**9**	**20.9**	**9**	**0.05505**	**13**	**8.1**	**13**	**0.02200**

1. Device Related Complications are defined as symptomatic or asymptomatic device related clinical events with potential adverse effects which require physician intervention.
2. Device Related Observations are defined as symptomatic or asymptomatic device related clinical events which do not require physician intervention.
3. The difference in the number of patients (N=158) and the number of leads included in adverse event calculations (N=161) is due the fact that one lead was replaced with another 1342T lead after the patient contaminated the sterile field, and two leads were replaced with active fixation leads, one due to repeated dislodgment and one due to difficulty with lead placement.
4. This rate is determined by dividing the number of adverse events by the cumulative implant duration (in months) for the given lead model.

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TABLE 8: VENTRICULAR LEAD RELATED ADVERSE EVENTS

	MODEL 1246T (CUMULATIVE IMPLANT DURATION = 330.72 MONTHS)				MODEL 1346T (CUMULATIVE IMPLANT DURATION = 790.44 MONTHS)			
DEVICE RELATED COMPLICATIONS[1]	NUMBER OF PATIENTS (N=80)	PERCENTAGE OF PATIENTS (%)	NUMBER OF LEADS (N=82)	ADVERSE EVENTS PER LEAD MONTH[4]	NUMBER OF PATIENTS[3] (N=215)	PERCENTAGE OF PATIENTS (%)	NUMBER OF LEADS[3] (N=216)	ADVERSE EVENTS PER LEAD MONTH[4]
Difficulty with Lead Placement	1	1.3	1	0.00302	1	0.5	1	0.00127
Cardiac Perforation	0	0	0	0.00000	1	0.5	1	0.00127
Lead Dislodgment	1	1.3	1	0.00302	1	0.5	1	0.00127
Loss of Capture	0	0	0	0.00000	1	0.5	1	0.00127
Increased Capture Thresholds	0	0	0	0.00000	2	0.9	2	0.00253
Decreased Sensing Thresholds	0	0	0	0.00000	2	0.9	2	0.00253
DEVICE RELATED OBSERVATIONS[2]	NUMBER OF PATIENTS (N=80)	PERCENTAGE OF PATIENTS (%)	NUMBER OF LEADS (N=82)	ADVERSE EVENTS PER LEAD MONTH[4]	NUMBER OF PATIENTS[3] (N=215)	PERCENTAGE OF PATIENTS (%)	NUMBER OF LEADS[3] (N=216)	ADVERSE EVENTS PER LEAD MONTH[4]
Difficulty with Lead Placement	0	0	0	0.00000	0	0	0	0.00000
Loss of Capture	0	0	0	0.00000	0	0	0	0.00000
TOTAL ADVERSE EVENTS	**2**	**2.6**	**2**	**0.00605**	**8**	**3.7**	**8**	**0.01012**

1. Device Related Complications are defined as symptomatic or asymptomatic device related clinical events with potential adverse effects which require physician intervention.
2. Device Related Observations are defined as symptomatic or asymptomatic device related clinical events which do not require physician intervention.
3. The number of leads is one greater than the number of patients as a result of one patient receiving a second model 1346T lead after unsuccessful attempted implant of previous model 1346T lead.
4. This rate is determined by dividing the number of adverse events by the cumulative implant duration (in months) for the given lead model

6. Clinical Event Analysis

Kaplan-Meier Survival Curves were generated for lead related complications and are presented in Figures 2-3 for atrial and ventricular leads, respectively.

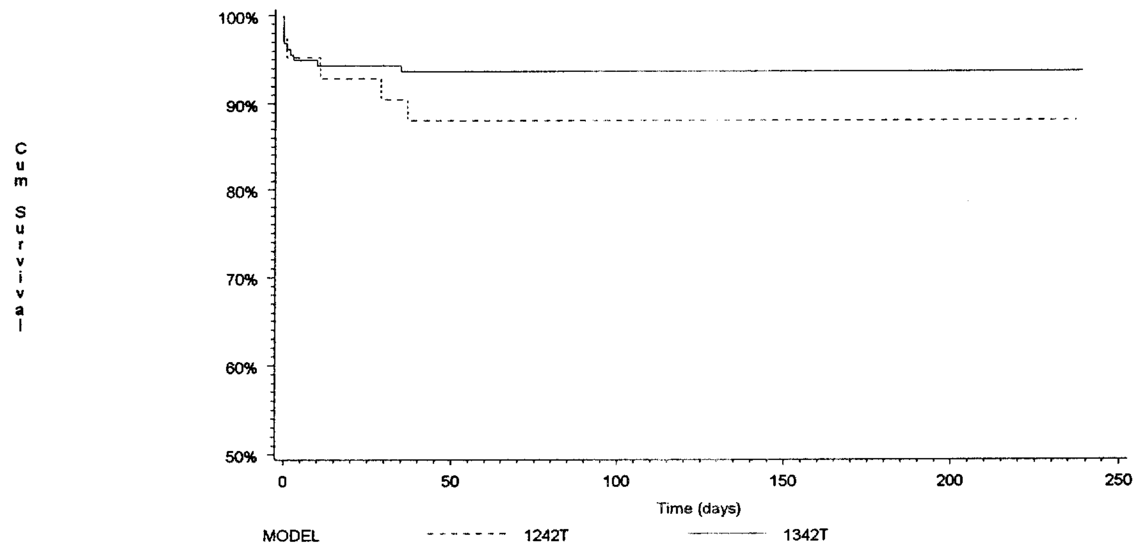


FIGURE 2: SURVIVAL CURVES FOR ATRIAL LEAD RELATED COMPLICATIONS

(Model 1242T Versus Model 1342T)

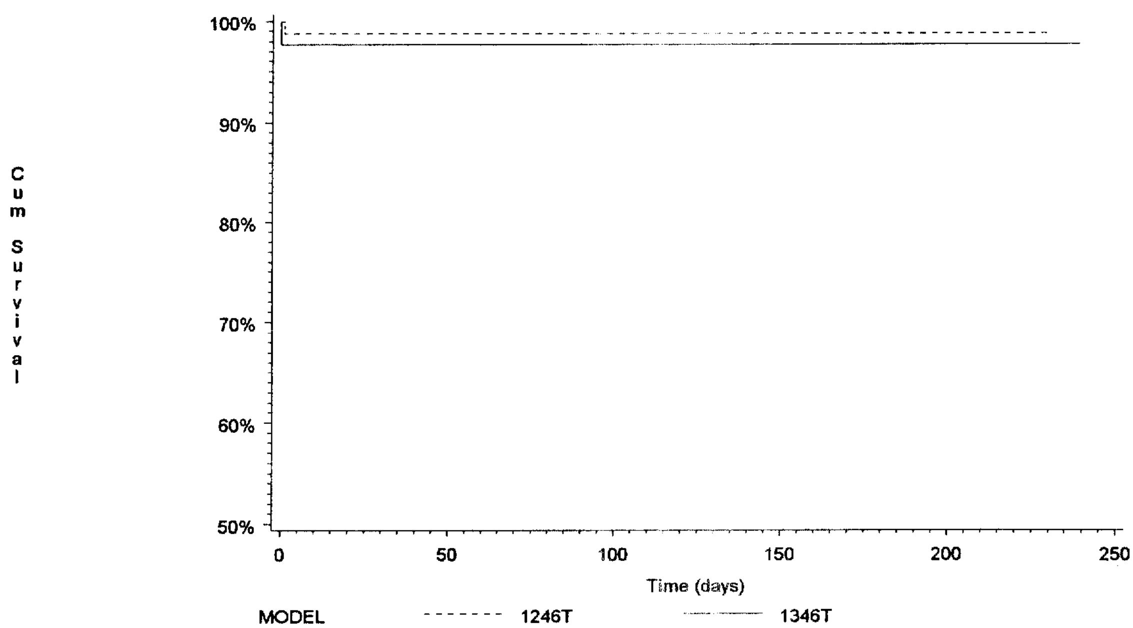


FIGURE 3: SURVIVAL CURVES FOR VENTRICULAR LEAD RELATED COMPLICATIONS

(Model 1246T Versus Model 1346T)

- The Kaplan-Meier Survival Curves estimate the probability, at each time t, that a particular lead model will be implanted at least t days without a lead related adverse event. Since it is only possible to determine standard errors in the survival curve at the uncensored observations, only approximate 95% confidence intervals for survival at the life length of the last uncensored observation are provided. Cumulative survival probabilities, as well as confidence intervals for the time t, in days, at which the confidence intervals were computed, are presented in Table 9 for each lead model.

TABLE 9: SUMMARY STATISTICS FOR SURVIVAL CURVES BY LEAD MODEL

LEAD MODEL	CHAMBER	TIME *t* (DAYS)	CUMULATIVE SURVIVAL PROBABILITY	95% CONFIDENCE INTERVAL
1242T	Atrial	37	0.8797	[0.78, 0.98]
1342T	Atrial	35	0.9365	[0.90, 0.97]
1246T	Ventricle	1	0.9873	[0.96, 1.00]
1346T	Ventricle	0	0.9766	[0.96, 1.00]

The Wilcoxon test was used to compare the survival curves for the atrial and ventricular control and investigational leads to determine if a statistically significant difference could be detected between the curves. The test detected no statistically significant differences at the 0.05 significance level. P-values from the Wilcoxon test are shown in Table 10 below.

TABLE 10: WILCOXON TEST RESULTS FOR SURVIVAL CURVE ANALYSIS

INVESTIGATIONAL VERSUS CONTROL LEAD	CHAMBER	P-VALUE
1242T versus 1342T	Atrial	0.2583
1246T versus 1346T	Ventricular	0.5562

XI. CONCLUSION DRAWN FROM THE STUDIES

A series of *in vitro* qualification tests performed for the model 1342T, 1346T, 1343K, and 1345K leads (as well as tests performed for the similar model 1242T, 1246T, 1245K, and 1245K leads) has demonstrated the mechanical integrity of the Passive Plus DX pacing leads and their ability to withstand stresses encountered during normal use.

Clinical investigations conducted with the model 1342T and 1346T leads have demonstrated that the presence of the MCRD in the distal electrode tip results in a statistically significant reduction in capture thresholds through three months post implant relative to a nearly identical lead without a steroid release mechanism. Clinical investigations were not conducted for the model 1343K, or 1345K lead, however the clinical study results for the 1342T/1346T are applicable 1343K, 1345K because the pacing electrode is identical.

Therefore, it is reasonable to conclude that the benefits of use of the device for the target population outweigh the risk of illness or injury when used as indicated in accordance with the directions for use. Additionally, clinical investigations have confirmed that the Passive Plus DX leads provide lower capture thresholds during the first three months post implant than a non-steroid control lead.

XII. PANEL RECOMMENDATIONS

Pursuant to section 515(f)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory System Devices Panel for review and recommendations because the information in the PMA substantially duplicated information previously reviewed by this panel.

XIII. FDA DECISION

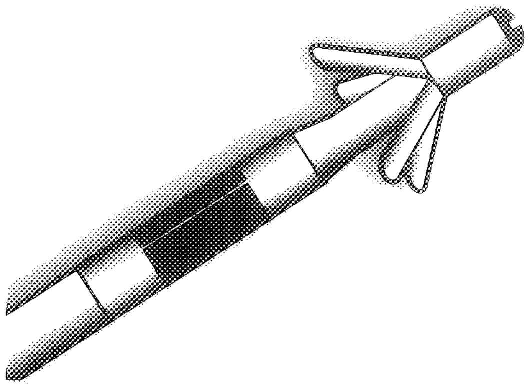
FDA recommends approval of the application with the condition that the manufacturer submit a final report for the results of distal tip flex testing when testing through 400 million cycles has been completed. FDA issued an approval order on January 29, 1998. The applicant's manufacturing facility was found to be in compliance with the device Good Manufacturing Practice regulations (21 CFR Part 820).

XIV. APPROVAL SPECIFICATION

Directions for Use:	See labeling.
Hazards to Health from Use of Device:	See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the labeling.
Post Approval Requirements and Restrictions:	See approval order.

The Approval Order, Summary of Safety and Effectiveness Data, and labeling can be found on the Internet at http: //www.fda.gov/cdrh/pmapage.html.

Pacesetter



PASSIVE PLUS® DX

Models 1342T, 1346T, 1343K, 1345K

Endocardial, Steroid-Eluting, Passive-Fixation Pacing Leads

USER'S MANUAL

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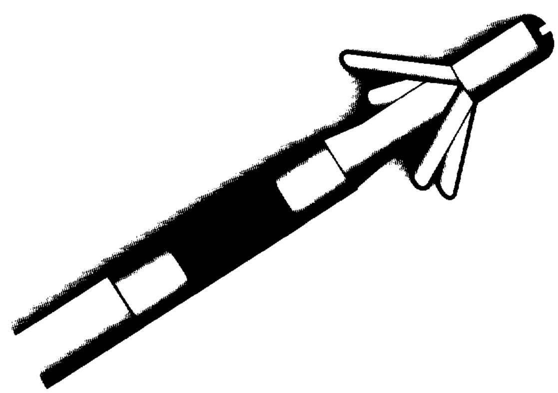
Pacesetter®



PASSIVE PLUS® DX

Models 1342T, 1346T, 1343K, 1345K

Endocardial, Steroid-Eluting, Passive-Fixation Pacing Leads

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Contents

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DEVICE DESCRIPTION

Passive Plus® DX leads are silicone-insulated, steroid-eluting, Titanium Nitride (TiN) coated, IS-1 compatible, endocardial pacing leads which may be either unipolar (Passive Plus 1343K, 1345K) or bipolar (Passive Plus 1342T, 1346T).

Passive Plus DX features passive fixation. Models 1342T/1346T and 1343K/1345K have a tine fixation feature. Models 1342T and 1343K are J-shaped leads intended for atrial placement, whereas Models 1345K and 1346T are straight leads intended for ventricular placement.

Table 1. Passive Plus DX Models and Features

Model	Features		
1342T	Bipolar	Tine	J/Atrial
1343K	Unipolar	Tine	J/Atrial
1345T	Unipolar	Tine	Straight/Ventricular
1346T	Bipolar	Tine	Straight/Ventricular

Passive Plus DX leads have a Monolithic Controlled-Release Device (MCRD) located in the tip electrode of the lead. The MCRD is a molded plug of silicone medical adhesive impregnated with 400 to 1000 micrograms of dexamethasone sodium phosphate (DSP). The steroid (DSP) decreases the inflammatory reaction of the heart during the acute stage (0-3 months post-implant) of patient recovery.

INDICATIONS/INTENDED USE

The Passive Plus DX lead is designed for use in combination with a compatible pulse generator to provide permanent pacing and sensing in either the atrium (Models 1342T or 1343K) or ventricle (Models 1346T or 1345K).

CONTRAINDICATIONS

The use of the Model 1342T, 1346T, 1343K or 1345K is contraindicated:

- in patients who are expected to be hypersensitive to a single dose of 1.0 milligram of dexamethasone sodium phosphate

The use of the Model 1346T or 1345K is also contraindicated:

- in the presence of tricuspid atresia and in patients with mechanical tricuspid valves.

WARNINGS

- ***Exercise extreme caution when testing leads.***
- ***Use only battery-powered equipment during lead implantation and testing to protect against fibrillation which may be induced by alternating currents.***
- ***Use only properly grounded line-powered equipment in the vicinity of the patient during the implant procedure.***
- ***Insulate lead connector pins from any leakage currents that may arise from line-powered equipment.***

PRECAUTIONS

- For single use only. Do not resterilize leads more than once.

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- Do not sterilize the lead using an autoclave, gamma radiation or ultrasonics. If sterilization is required, see page 9.
- Before opening the lead package, confirm that it is compatible with the pulse generator to be implanted.

STORAGE AND HANDLING

- The lead should be stored at temperatures between -5° C (23° F) and 55° C (131° F).
- The lead conductor and its insulating sheath may be damaged if subjected to extreme mechanical stress.
- Do not stretch, crush, kink or bend the lead as leads may be damaged by improper handling before and during implant or by excessive mechanical stress post-implantation.
- Do not bring the lead into contact with sharp objects which could puncture or otherwise compromise the insulation.
- Handle the lead only with powderless, sterile surgical gloves.
- Avoid handling the lead with any surgical tools such as hemostats, clamps or forceps.
- Leads have an electrostatic affinity for particulate matter; do not expose them to lint, dust or other such materials.
- Avoid touching or handling the lead tip electrode itself.
- Do not immerse the lead body in mineral oil, silicone oil or any liquid other than sterile saline or injectable fluid.
- Do not immerse the tip electrode in any fluid prior to implantation. Immersion of the electrode may cause a small amount of steroid to be prematurely eluted.

IMPLANTATION

- Lead implantation should be performed only when proper emergency facilities for cardioversion and/or defibrillation are available.
- If subclavian venipuncture is used for lead introduction, it is important to insert the lead as lateral as possible during entry of the lead into the vein.
- Perforation of the atrial or ventricular wall may cause phrenic nerve stimulation, diaphragmatic stimulation or in some instances, cardiac tamponade. Phrenic nerve or diaphragmatic stimulation may also be a result of lead position.
- Failure to use the anchoring sleeve may result in damage to the lead's insulation, conductor coil or both.
- The manipulation of any and all hardware while in the vascular system should be performed only under continuous fluoroscopic monitoring.

ADVERSE EVENTS

The Passive Plus DX clinical study involved 158 Model 1342T leads and 215 Model 1346T leads. Cumulative implant duration for each lead model is as follows:

- 1342T: 17,988 days (mean implant duration 113.8 days, range 0 to 239 days)

- 1346T: 24,061 days (mean implant duration 111.9 days, range 1 to 239 days)

Observed Adverse Events

Device-related adverse events reported during the study are summarized in Tables 2 and 3.

A total of eight patient deaths were reported. None of these deaths were judged to be device or lead-related.

Table 2. Passive Plus DX Model 1346T Ventricular Leads
(Cumulative Implant Duration = 790.44 Months)

Device-Related Adverse Events[1]	Number of Patients[2] N=215	Percentage of Patients (%)	Number of Leads[2] N=216	Adverse Events Per Lead Month[3]
Difficulty with Lead Placement	1	0.5	1	0.00127
Cardiac Perforation	1	0.5	1	0.00127
Lead Dislodgment	1	0.5	1	0.00127
Loss of Capture	1	0.5	1	0.00127
Increased Capture Thresholds	2	0.9	2	0.00253
Decreased Sensing Thresholds	2	0.9	2	0.00253
Total Adverse Events	**8**	**3.7**	**8**	**0.01012**

1. Device-related adverse events are defined as symptomatic or asymptomatic device-related clinical events with potential adverse effects which require physician intervention.
2. The number of leads is one greater than the number of patients as a result of one patient receiving a second model 1346T lead after unsuccessful attempted implant of a previous model 1346T lead.
3. This rate is determined by dividing the number of adverse events by the cumulative implant duration (in months) for the given lead model.

Table 3. Passive Plus DX Model 1342T Atrial Leads
(Cumulative Implant Duration = 590.93 Months)

Device-Related Adverse Events[1]	Number of Patients[2] ~~N=160~~ 158	Percentage of Patients (%)	Number of Leads[2] N=161	Adverse Events Per Lead Month[3]
Difficulty with Lead Placement	1	0.6	1	0.00169
Lead Dislodgment	9	5.6	9	0.01523
Loss of Capture	1	0.6	1	0.00169
Loss of Sensing	2	1.3	2	0.00338
Total Adverse Events	**13**	**8.1**	**13**	**0.02200**

1. Device-related adverse events are defined as symptomatic or asymptomatic device-related clinical events with potential adverse effects which physician intervention. require
2. The difference in the number of patients (N=158) and the number of leads included in adverse event calculations (N=161) is due to the fact that one lead was replaced with another 1342T lead after the patient contaminated the sterile field, and two leads were replaced with active fixation leads, one due to repeated dislodg~~e~~ment and one due to difficulty with lead placement.
3. This rate is determined by dividing the number of adverse events by the cumulative implant duration (in months) for the given lead model.

POTENTIAL ADVERSE EVENTS

Adverse events which may occur with this type of device, including those listed above, include:

- cardiac tamponade
- diaphragmatic stimulation
- embolism
- excessive bleeding
- induced atrial or ventricular ectopy
- infection
- loss of pacing and or sensing due to dislodgment or mechanical malfunction of the pacing lead
- phrenic nerve stimulation
- thrombosis

Acute complications reported with direct subclavian venipuncture include pneumothorax, hemothorax, laceration of the subclavian artery, arteriovenous fistula, neural damage, thoracic duct injury, cannulation of other vessels, massive hemorrhage and, rarely, death.

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Clinical Study

A multi-center, prospective, randomized, controlled clinical study was conducted to compare capture thresholds of the Model 1342T atrial lead and the Model 1346T ventricular lead through three months post-implant to those of the commercially available, non-steroid passive-fixation Model 1242T atrial lead and Model 1246T ventricular lead, respectively. Patients were randomized to receive either a 1342T or a 1242T lead in the atrium and either a 1346T or a 1246T lead in the ventricle using a 3:1 randomization ratio (three Model 1342T leads to each Model 1242T lead; three Model 1346T leads to each Model 1246T lead).

Lead electrical performance characteristics, including capture thresholds, sensing thresholds and lead impedances, were evaluated at implant and at 14 days (± 4 days), 30 days (± 7 days), 90 days (± 14 days) and 180 days (± 30 days) post-implant. A total of 495 leads were implanted in 306 patients. Of the 495 leads implanted, 42 were Model 1242T, 158 were Model 1342T, 80 were Model 1246T and 215 were Model 1346T. Of the 306 patients, a total of 164 (54%) were males and 142 (46%) were females. The age of the patient population at the time of implant ranged from 20 to 92 years, with a mean of 74 ± 11 years. Statistical comparisons of patient demographics were made between patients with Models 1242T/1246T leads and patients with Models 1342T/1346T leads, respectively (Table 6 on page 8). Comparisons indicated no statistically significant differences between the patient populations for patient gender, patient age, primary indication for pacing, physiologic conditions which could affect pacing thresholds or medications which could affect pacing thresholds.

Analysis of the clinical data demonstrated that the presence of the Monolithic Controlled-Release Device (MCRD) in the distal tip electrode of the 1342T/1346T leads results in a statistically significant reduction in capture thresholds through three months post-implant relative to the non-steroid passive-fixation 1242T/1246T leads (Tables 5-6).

Table 4. Comparison of patients receiving 1242T/1246T Leads and 1342T/1346T leads

Variables	Atrial 1242T	Atrial 1342T	Atrial Statistics	Ventricular 1246T	Ventricular 1346T	Ventricular Statistics
Gender Male Female	 21 (50%) 21 (50%)	 88 (55.7%) 70 (44.9%)	 Fisher's Exact Test p = 0.602	 44 (55%) 36 (45%)	 117 (54.4%) 98 (45.6%)	 Fisher's Exact Test p = 1.000
Age(years): Range Mean STD	 38.2- 90.8 72.4 11.7	 37.4 - 90.0 74.4 10.3	 t = -1.0728 d.f. 198 p = 0.2847	 20.8 - 92.3 74.1 13.4	 33.5 - 92.0 74.3 9.8	 t = -0.1105 d.f. 112.4 p = 0.9122
Primary Indication Sick Sinus: Reported Normal *	 13 (31.0%) 29 (69.1%)	 48 (30.4%) 110 (69.6%)	 Fisher's Exact Test p = 1.000	 27 (33.8%) 53 (66.3%)	 62 (28.8%) 153 (71.2%)	 Fisher's Exact Test p = 0.476
Sinus Bradycardia: Reported Normal *	8 (19.1%) 34 (81.0%)	28 (17.7%) 130 (82.3%)	Fisher's Exact Test p = 0.824	10 (12.5%) 70 (87.5%)	35 (16.3%) 180 (83.7%)	Fisher's Exact Test p =0.472
Heart Block: Reported Normal *	15 (35.7%) 27 (64.3%)	79 (50.0%) 79 (50.0%)	Fisher's Exact Test p = 0.118	30 (37.5%) 50 (62.5%)	93 (43.3%) 122 (56.7%)	Fisher's Exact Test p = 0.426
PCAPT: Condition(s) None Not Reported **	 7 (16.7%) 35 (83.3%) 0	 31 (19.8%) 126 (80.3%) 1	 Fisher's Exact Test p = 0.826	 17 (21.3%) 63 (78.8%) 0	 43 (20.2%) 170 (79.8%) 2	 Fisher's Exact Test p = 0.871
MAPT: Not reported at Implant Reported at Implant	 34 (81.0%) 8 (19.1%)	 125 (79.1%) 33 (20.9%)	 Fisher's Exact Test p = 1.000	 60 (75%) 20 (25%)	 173 (80.5%) 42 (19.5%)	 Fisher's Exact Test p = 0.336
Total Patients per Lead Group	**42**	**158**		**80**	**215**	

* Normal Function, relative to the corresponding primary indication
** Not included in statistical analysis
PCAPT = physiological conditions affecting pacing thresholds
MAPT = medications affecting pacing thresholds

Table 5. Atrial Capture Thresholds (Volts) at 0.4 ms Pulse Width

Follow-Up	**Unipolar: mean ± SD[1] (N)[2]**			**Bipolar: mean ± SD[1] (N)[2]**		
	1242T	**1342T**	P-value[3]	**1242T**	**1342T**	P-value[3]
Implant	0.7 ± 0.3 N = 39	0.9 ± 0.4 N=141	0.0672	0.8 ± 0.3N = 39	0.8 ± 0.4 N = 141	0.6729
Two Weeks	2.0 ± 1.3 N = 32	1.0 ± 0.9 N = 129	0.0001	2.0 ± 1.3 N = 33	1.0 ± 1.0 N = 131	0.0001
One Month	1.9 ± 1.1 N = 28	0.9 ± 0.8 N = 120	0.0001	2.0 ± 1.3 N = 29	1.0 ± 0.7 N = 120	0.0001
Three months	1.6 ± 0.7 N = 20	1.0 ± 1.0 N = 71	0.0001	1.4 ± 0.7 N = 19	1.0 ± 0.9 N = 70	0.0004

1. SD = standard deviation
2. N = sample size
3. Wilcoxon Rank Sum Test

Table 6. Ventricular Capture Thresholds (Volts) at 0.4 ms Pulse Width

Follow-Up	**Unipolar: mean ± SD[1] (N)[2]**			**Bipolar: mean ± SD[1] (N)[2]**		
	1246T	**1346T**	**P value[3]**	**1246T**	**1346T**	**P value[3]**
Implant	0.6 ± 0.3 N = 78	0.6 ± 0.3 N = 208	0.4055	0.7 ± 0.4 N = 78	0.7 ± 0.3 N = 209	0.7521
Two Weeks	1.3 ± 0.6 N = 68	0.8 ± 0.4 N = 189	0.0001	1.6 ± 0.8 N = 69	0.9 ± 0.5 N = 192	0.0001
One Month	1.5 ± 0.7 N = 75	0.9 ± 0.5 N = 174	0.0001	1.7 ± 0.7 N = 75	1.0 ± 0.5 N = 175	0.0001
Three months	1.4 ± 0.5 N = 48	0.9 ± 0.4 N = 105	0.0001	1.6 ± 0.6 N = 48	1.0 ± 0.4 N = 106	0.0001

1. SD = standard deviation
2. N = sample size
3. Wilcoxon Rank Sum Test

Detailed Device Description

Features of the Passive Plus DX lead include:

- Passive Fixation – the lead tip wedges under the trabeculae
- Steroid Elution – Steroid is slowly released through the tip electrode upon contact with body fluid. The drug is intended to promote low chronic pacing thresholds by suppressing the inflammation at the electrode-tissue interface.
- Fast-Pass® Coating – Molecular coating creates a highly lubricious surface.

The Passive Plus DX pacing leads are designed for use with implantable pulse generators for long-term cardiac pacing. They are passed transvenously to the heart. Once properly fixated, the pacing lead is connected to the pulse generator.

The steroid drug which is released slowly promotes low acute to chronic pacing threshold by suppressing the inflammation response to a foreign body.

The lead conducts stimulating pulses from the pulse generator to the heart and, in demand pacing modes, delivers electrical information on the intrinsic cardiac activity to the sense amplifiers of the pulse generator.

The Passive Plus DX is available in both unipolar and bipolar models. 1343K and 1345K unipolar leads have one conductor that terminates at the tip electrode. 1342T and 1346T bipolar leads have two conductors: one terminating at the tip electrode (cathode) and the other at the larger, microporous titanium nitride-coated ring electrode (anode) approximately 11 millimeters from the tip.

Passive Plus DX leads comply with IS-1 connector standard ISO 5841-3.

All implantable pacing leads from Pacesetter are made of biocompatible materials.

Note. *A pacing lead explanted for any reason should never be implanted in another patient.*

Note. *Lead/pulse generator compatibility should be confirmed with the pulse generator and/or lead manufacturer(s) prior to implantation of a pacing system.*

Package Contents

The contents of the package are sterile. Each package contains:

- One passive-fixation pacing lead with anchoring sleeve attached
- One vein lifter
- Stainless steel stylets.

Keep the lead tip electrode protector (if provided) in place until the lead is ready to be implanted.

Sterilization

The lead package has been sterilized with ethylene oxide for direct introduction of the inner tray into the surgical field. Before the package is opened, inspect it visually for any damage that may have compromised sterility.

If resterilization is necessary, place the lead and accessories in a gas-permeable package and resterilize in ethylene oxide. The sterilizer temperature should not exceed 52 °C (125 °F). After sterilization, allow sufficient time for the complete aeration of ethylene oxide residuals prior to implantation. This process may be shortened by forced ventilation. Use biological controls to verify the effectiveness of the resterilization.

CAUTION

- ***Do NOT sterilize the lead using an autoclave, gamma radiation or ultrasonics.***
- ***Do not re-sterilize the lead more than once.***

OPERATING INSTRUCTIONS

Lead Selection

There are many factors to take into account when choosing a pacing lead. The first is compatibility with the pulse generator, which may be verified by consulting with your Pacesetter representative and, if applicable, the pulse generator manufacturer.

Many pulse generators offer programmable polarity, meaning that pacing and/or sensing may be programmed to function in a unipolar or bipolar configuration. The bipolar, steroid-eluting lead may function in a unipolar or bipolar configuration depending on how the pulse generafor is programmed.

Some pulse generators offer independently programmable polarity for both pacing and sensing. Unipolar pacing produces a relatively large pacing artifact that is easily recognizable on a surface ECG. However, unipolar pacing may cause skeletal muscle stimulation in the pocket area. Unipolar sensing may be more sensitive to extracardiac signals than bipolar sensing.

Bipolar pacing is much less likely to cause muscle stimulation than unipolar pacing. However, the bipolar pacing spike is usually very small and may be difficult to discern on a surface ECG. Bipolar sensing is known to be much less affected by myopotentials and external interference than unipolar sensing.

Implantation

The goal of any lead implantation is to minimize mechanical stresses on the pacing lead while simultaneously maximizing the lead's electrical contact with cardiac tissue.

CAUTION

Lead implantation should be performed only under continuous fluoroscopic monitoring and when proper emergency facilities for cardioversion and/or defibrillation are available.

Lead Preparation

It is important that the implanting physician completely understand the mechanical operation of this lead before surgery.

LEAD INTRODUCTION

There are several venous routes for passing the endocardial pacing lead, including the right or left cephalic, subclavian, axillary or internal and external jugular veins. Veins may be accessed using the cut-down or venipuncture method.

CAUTION

The manipulation of any and all intravascular hardware should be performed only under continuous fluoroscopic monitoring.

Cut-down technique

Except for the subclavian vein, any of the other veins may be used for the cut-down technique. In the cut-down technique, the desired vein is identified and a small incision made for lead insertion.

The vein lifter tool, included in the lead package, can be used to lift and dilate the vein, facilitating lead insertion.

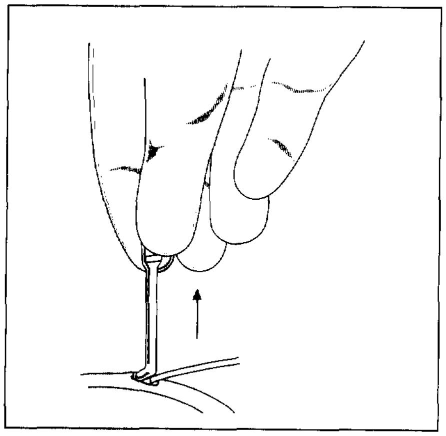

Figure 1

When using the cut-down technique, the vein lifter facilitates lead introduction. Insert its tapered end into the vein and gently lift.

Subclavian puncture method

The subclavian puncture method requires the use of a percutaneous lead introducer. Identify and distend the subclavian vein and use the needle in the introducer kit to puncture the vein (see Figure 2). Take the guide wire and advance the J straightener over the J shaped tip to facilitate placement of the guide wire into the needle and thus into the vein. Remove the needle, leaving the guide wire in place. The tip will resume its slightly curved shape, protecting the tip during transvenous passage.

CAUTION

When subclavian venipuncture is used for lead introduction, it is important to insert the lead as lateral as possible during entry of the lead into the vein.

Note. *The normal status of the subclavian vein often renders it difficult to puncture unless it is distended. This can be accomplished by raising the patient's legs to a 45° angle or by using the Trendelenburg position. The vein will be much easier to locate if the patient is well hydrated.*

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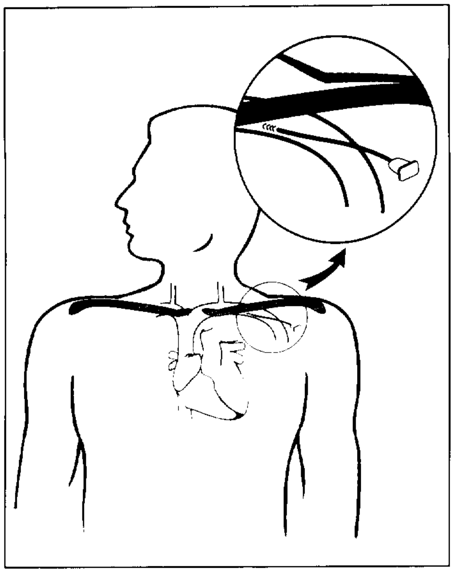

Figure 2

Next, advance the dilator and sheath with a rotating motion over the guide wire and into the vein. To remove the dilator, hold the T-handle of the sheath and rotate the dilator and its locking clip counterclockwise. (These instructions assume the use of a Pacesetter introducer. If another type of introducer is used, follow the manufacturer's instructions.) Retract the guide wire and dilator, leaving the sheath in position.

Now, introduce the pacing lead with inserted stylet into the sheath and advance it into position. See "Ventricular Lead Placement" on page 13 and "Atrial Lead Placement" on page 14.

Note. *When retracting the guide wire and dilator in the subclavian puncture technique, manually compress or cover the opening of the introducer sheath to avoid inadvertent air aspiration.*

When the lead is properly positioned, remove the sheath by using the tabs on either side to tear the sheath down and away. For more information on the subclavian puncture method using the percutaneous introducer kit, please consult the introducer manual.

Introduction of Two Leads

Dual-chamber pacemakers require the implantation of two leads – one in the atrium and the other in the ventricle. Two leads may be implanted in one of three ways:

- making two venipunctures
- making one puncture and using an introducer sufficiently large to accommodate both leads
- using the retained guide wire technique.

The retained guide wire technique, the most commonly used method, involves using the introducer in one venipuncture but removing the guide wire and dilator together before the lead is inserted into the sheath. For the second lead, the guide wire (and straightener as tip deflector, if desired) is reinserted down the first sheath; the first sheath is then removed and the second sheath placed over the guide wire. The guide wire and dilator are then removed as a unit and the second lead is inserted through the second sheath.

Stylets

Each Passive Plus DX pacing lead comes supplied with several stylets. When inserted into the pacing lead, the stylet gives the lead sufficient rigidity to be manipulated easily through the vein and into the heart.

A red knob on the stylet designates the soft stylet, while a blue knob identifies the firmer stylet. Stylet length is indicated on the knob.

Insert the stylet into the lead before lead introduction and remove the stylet before testing the lead for mechanical stability or making intraoperative measurements.

Lead Placement

Ventricular Lead Placement

After introducing the lead, advance it cautiously under fluoroscopic observation into the right atrium. Remove the straight stylet.

Take a new stylet, curve it gently, and insert it into the lead. This curve helps the lead negotiate its way across the tricuspid valve as it is gently manipulated into the right ventricle. Once the lead is in the right ventricle, retract the stylet slightly to minimize the chance of cardiac wall perforation.

Note. *Avoid contaminating the stylet with blood. Blood introduced into the core of the lead via the stylet may cause the stylet to bind and prevent it from being advanced or manipulated. If this occurs, remove the lead and replace it with a new lead.*

An alternate lead placement method involves using the straight stylet with the lead in the right atrium. Retract the stylet a few centimeters so the lead tip is floppy. Gently advance sufficient lead within the right atrium so that a loose loop forms. Under fluoroscopic observation, allow this loop to flip or prolapse through the tricuspid valve (so that the loop passes through the valve first, drawing the tip through afterward).

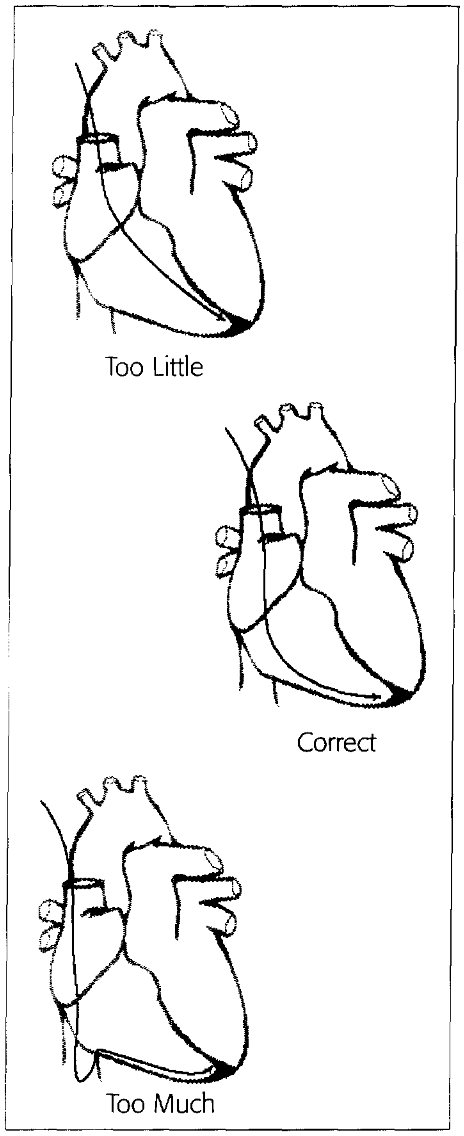

Figure 3

Once the lead is in the right ventricle, advance it cautiously toward the right ventricular apex. To avoid the inadvertent placement of the lead in the coronary sinus, it may be useful to advance the lead through the right ventricle and into the pulmonary artery, followed by gently withdrawing the lead until the tip falls into the apex.

Under fluoroscopic observation, verify that the lead has entered the pulmonary artery. Replace the curved stylet with a straight stylet (if necessary) and then gently pull the lead back into the right ventricle.

Proper positioning of the lead requires that it wedge under the trabeculae and resist removal under gentle traction. Under fluoroscopy, the lead tip should point anteriorly toward the apex with the tip showing a slight curve (Figure 3).

To verify that the lead is not pointing posteriorly, which usually indicates that it is in the coronary sinus, lateral fluoroscopy may be necessary. The lead should be wholly in the cardiac shadow on AP fluoroscopy. If it is not, the lead may be in the coronary sinus or one of the coronary veins or may have perforated the cardiac wall. (If the lead is unintentionally in the coronary sinus or a coronary vein or is believed to have perforated, gently retract it and reposition it.)

When the lead is in the proper position, fully withdraw the stylet prior to assessing capture and sensing thresholds.

Atrial Lead Placement

After introducing the lead, advance it cautiously toward the heart under fluoroscopic observation. If resistance is encountered, pull the lead back a short distance and readvance it, repeating this procedure as often as necessary. This will cause the J to form and may make advancing the lead more difficult. This is appropriate for the ventricular lead.

Advance the lead. Once past the obstruction, cautiously readvance the stylet. Guide the lead into the right atrium just below the superior vena cava. Use fluoroscopy to verify proper position.

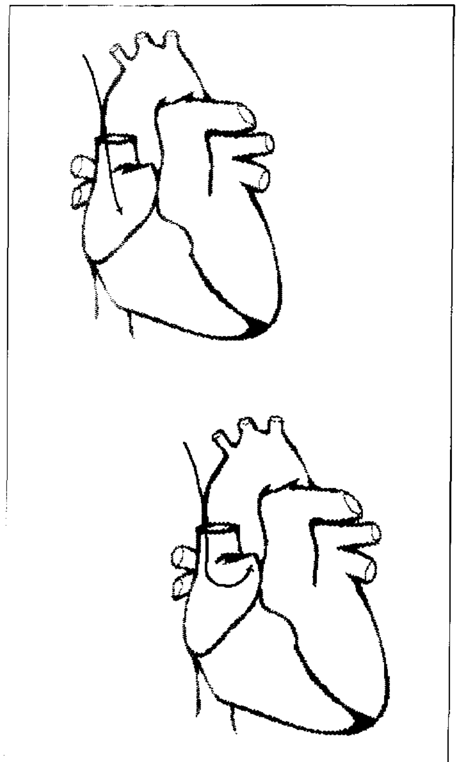

Figure 4

When the lead reaches the junction of the right atrium and the superior vena cava, hold the stylet stationary and under fluoroscopic observation, advance the lead over the stylet into the right atrium. The lead should point in an anteromedial direction. (See top of Figure 4.) Then gently retract the stylet several centimeters further so that the lead's distal end resumes its J-shape. (See lower portion of Figure 4.) This should allow the lead tip to lodge in the atrial appendage.

When the lead is properly placed, its J- curve should straighten somewhat when the lead is slightly retracted. Under AP fluoroscopy, the lead tip should point medially toward the left. It should sway slightly from side to side with each atrial contraction (when there is AV synchrony). A loose J-shape of the lead is preferred, as shown in Figure 5.

If the lead is properly positioned, a very slight rotation of the lead will be seen to change the position of the body of the J, but not the tip.

Some physicians assess proper lead tension by having the patient breathe deeply several times. On maximal expiration, the J will appear almost closed; on maximal inspiration, the J will open to almost an L shape.

When the lead is in the proper position, fully withdraw the stylet.

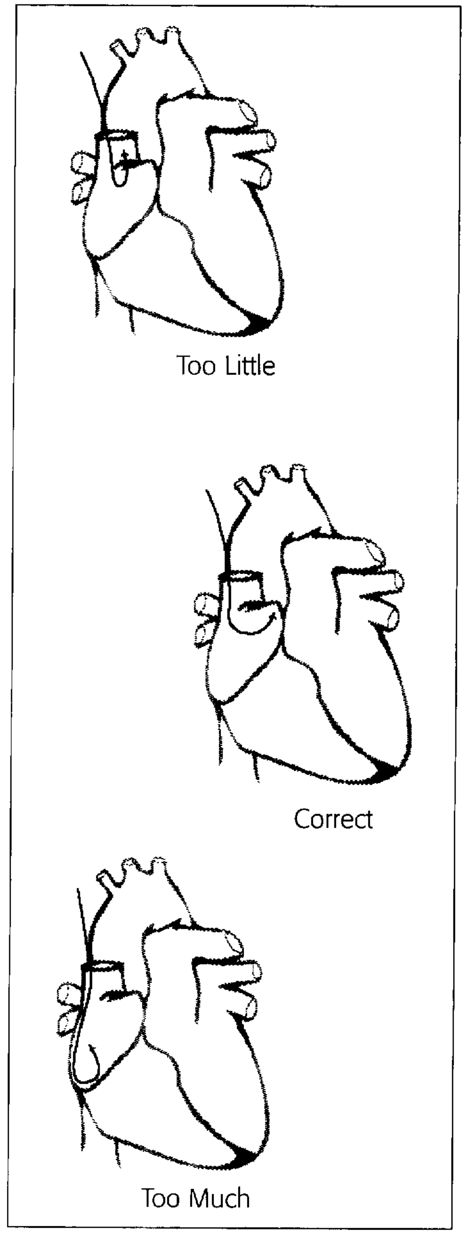

Figure 5

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Intraoperative Measurements

It is important to verify stimulation threshold and sensing capability during implantation. A measuring device such as a pacing system analyzer (PSA) is recommended for these electrical measurements.

WARNING
A pacing lead inserted into the heart presents a direct, low-impedance pathway for current flow to the myocardium. Use only battery-powered test equipment for electrical measurements.

Connection to Pacing System Analyzer

Remove the percutaneous lead introducer and stylet from the lead once the lead is in what is believed to be a suitable location.

Use the PSA cables to connect the terminal pin of the implanted pacing lead to the analyzer. It is recommended that the PSA be programmed off or to a passive setting while connections are being made.

For a unipolar lead, connect the black PSA cable (negative pole or cathode) to the lead connector's terminal pin. This terminal pin connects to the distal tip electrode. Connect the red or positive PSA cable (anode) to an indifferent electrode. This indifferent electrode should be placed in direct contact with tissue at the pocket location.

Note. *Do not use an alligator clip as an indifferent electrode by connecting it directly to tissue. This causes tissue trauma and provides a very small surface area, giving incorrect voltage thresholds and impedance measurements. Connect the indifferent cable to either a special indifferent electrode or to a piece of sterilized surgical equipment with a large surface area (such as the metal handle of a scalpel) and place this in the pocket.*

For a bipolar lead with an in-line connector, connect the black PSA cable (negative) to the lead connector's terminal pin and the red PSA cable (positive) to the lead connector's terminal ring (associated with the anode ring electrode).

Note. *Carefully apply alligator clips to the in-line bipolar terminal pin to avoid damaging the insulation between terminal pins.*

For more information on the use of the PSA, please refer to the PSA manual.

Stimulation Threshold

As a general rule, the stimulation threshold (the output values needed to reliably and consistently capture the heart) is lowest in the acute phase. The stimulation threshold can be expected to increase during the next several weeks after implant and then remain at the new value or decrease slightly to stabilize, typically at one to three months post-implantation.

Note. *Thresholds are measured using either pulse amplitude (voltage) or pulse width (milliseconds). Doubling the pulse amplitude quadruples the energy output of the pulse generator, while doubling the pulse width doubles the energy output.*

When selecting output parameter values for the pulse generator (pulse amplitude and pulse width) make every effort to obtain the lowest possible settings and provide an adequate safety margin. The safety margin assures that capture will occur even if the patient's threshold increases over time. A safety margin of two to three times the voltage stimulation threshold is generally considered adequate in a chronic or stable system. Actually, it is common to use higher safety margins.

Once lead maturation has occurred, an adequate safety margin can be maintained with lower output settings as the threshold is not likely to change markedly. Reducing the output at that time can increase pulse generator longevity.

Using a 0.4 ms pulse width and assuming a 500-ohm load, it should be possible to obtain the acute stimulation thresholds listed in Table 7. If the threshold values are greater than the recommended values, reposition the lead.

Table 7. Acute Stimulation Thresholds

Atrial	<1.5 V <3.0 mA
Ventricular	<1.0 V <2.0 mA

Sensing Threshold

Verify the sensing threshold at implant. The sensing threshold is the lowest sensitivity setting of the pulse generator's sensing circuitry that can appropriately sense an intrinsic endocardial signal.

The sensing threshold is often defined by the pulse generator's sensitivity parameters (mV setting). An intrinsic signal measuring 5.5 mV will be sensed when pulse generator sensitivity is programmed to 5.0 mV, but will not be sensed when sensitivity is set at 8.0 mV.

Note. *A higher mV setting decreases sensitivity, while a lower mV setting increases sensitivity.*

Recommended acute sensing thresholds are shown in Table 8. If the sensing threshold falls below these guideline numbers, the lead should be repositioned.

Table 8. Acute Sensing Thresholds

Atrial	>2.0 mV
Ventricular	>5.0 mV

When trying to determine an appropriate sensing signal, it is possible that an optimal signal cannot be found. This could lead to either undersensing (failure to sense an appropriate signal) or oversensing (sensing an inappropriate signal). For bipolar programmable pulse generators, it may be useful to examine the intracardiac electrogram for unipolar and bipolar configurations to evaluate whether one signal is better than the other. If both signals are poor, a bipolar sensing configuration is generally preferable since it minimizes oversensing.

Mechanical Stability

There are several techniques that can be used to verify the mechanical stability of the lead. One method involves setting an external pacemaker or the pacing system analyzer (PSA) to a pulse amplitude of 0.1–0.5 V above the stimulation threshold and having the patient breathe deeply or cough while verifying with both fluoroscopy and the ECG that the lead remains stable and capture is maintained.

For atrial leads, the external pacemaker or pacing system analyzer (PSA) should be programmed to a rapid atrial rate and lead stability should be checked by fluoroscopy and the ECG.

Concomitant with an evaluation of stability, evaluate the patient for diaphragmatic stimulation. Use the external pacemaker or pacing system analyzer to program a pulse amplitude of 10 V while checking that no diaphragmatic stimulation occurs and verifying with fluoroscopy and the ECG that the lead remains stable. If diaphragmatic stimulation occurs at this high output setting, it is recommended that the lead be repositioned (even if diaphragmatic stimulation does not occur at the lower stimulation threshold voltage, because future reprogramming of the pulse generator may someday require a high voltage output setting).

Anchoring the Lead

Once the lead has achieved a stable mechanical position with good thresholds, securely anchor the lead at or near the venous entry site using a nonabsorbable synthetic suture. First secure the anchoring sleeve to the underlying tissue, then recheck lead position visually and under fluoroscopy (to prevent twisting of the lead and identify inadvertent retraction or advancement of the lead). Finally, tie the ligature around the anchoring sleeve to secure the lead in place.

Note. *Do not tie the suture around the anchoring sleeve and lead too tightly, as this may result in excessive stress applied to the lead body.*

CAUTION

Use the anchoring sleeve to distribute the tension created by the suture. Failure to use the anchoring sleeve may result in damage to the lead's insulation or conductor coil.

Chronic Repositioning

It is generally recommended that a chronically implanted endocardial pacing lead not be repositioned except in special circumstances.

If it is necessary to abandon an indwelling pacing lead, remove its connector pin from the pulse generator and cap the lead using the standard cap of the lead manufacturer. It is not recommended to cut an indwelling pacing lead; this may cause the insulation to separate from the conductor coil and leave an exposed wire in the body.

Lead Extraction

Infection of the pacemaker system, particularly sepsis, generally requires the removal of both the pulse generator and the lead(s).

Note. *If a pacing lead must be removed due to infection or other serious reason, great care should be exercised as lead extraction carries with it clinical risk.*

If the lead or any portion of it is extracted, return it to Pacesetter.

SERVICE

Members of the Pacesetter Technical Services Department are available to provide technical consultation 24 hours every day. This service can be obtained by dialing 1 800 722 3774 or by faxing messages to 1 818 362 7182. Additionally, highly trained sales and service professionals are located worldwide to assist you.

ST. JUDE MEDICAL

CARDIAC RHYTHM MANAGEMENT DIVISION

15900 Valley View Court
Sylmar, CA 91342 USA
800/777-2237
818/362-6822

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